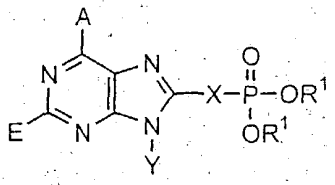
We claim:

1. A compound of formula 1:



wherein

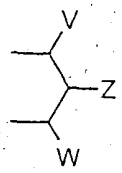
A is selected from the group consisting of $-NR^8_2$, $NHSO_2R^3$, $-OR^5$, $-SR^5$, halogen, lower alkyl, $-CON(R^4)_2$, guanidine, amidine, -H, and perhaloalkyl;

E is selected from the group consisting of -H, halogen, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or together with Y forms a cyclic group including cyclic alkyl, heterocyclic, and aryl;

Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;

R^1 is independently selected from the group consisting of -H, alkyl, aryl, alicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl, alkylaryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, alkyl-S-C(O)R^3, alkyl-S-S-alkylhydroxy, and alkyl-S-S-S-alkylhydroxy, or together R^1 and R^1 are -alkyl-S-S-alkyl to form a cyclic group, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -R^9; or

together V and Z are connected to form a cyclic group containing 3-5 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected to form a cyclic group containing 3 carbon atoms substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, and aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of -CH_2OH, -CH_2OCOR^3, -$CH_2OC(O)SR^3$, -$CH_2OCO_2R^3$, -SR^3, -$S(O)R^3$, -CH_2N_3, -$CH_2NR^2_2$, -CH_2Ar, -CH(Ar)OH, -$CH(CH{=}CR^2R^2)OH$, -$CH(C{\equiv}CR^2)OH$, and -R^2;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is -R^2, then at least one of V and W is not -H or -R^9;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and -$C(O)R^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, -$C(O)R^{10}$, or together they form a bidendate alkyl;

R^9 is selected from the group consisting of alkyl, aralkyl, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

2. The compounds of claim 1 with the proviso that R^1 is not lower alkyl of 1-4 carbon atoms.

3. The compounds of claim 1 wherein A is selected from the group consisting of $-NR^8_2$, halogen, lower alkyl, lower perhaloalkyl, and lower alkoxy.

4. The compounds of claim 1 wherein E is -H, halogen, lower perhaloalkyl, -CN, lower alkyl, lower alkoxy, and lower alkylthio.

5. The compounds of claim 1 wherein X is selected from the group consisting of alkylamino, alkyl, alkynyl, alkoxyalkyl, alkylthio, aryl, 1,1-dihaloalkyl, carbonylalkyl, heteroaryl, alkylcarbonylamino, and alkylaminocarbonyl.

6. The compounds of claim 5 wherein X is alkyl substituted with 1 to 3 substituents selected from the group consisting of halogen, phosphonate, $-CO_2H$, $-SO_3H$, and -OH.

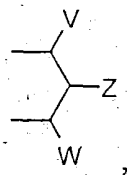
7. The compounds of claim 5 wherein X is selected from the group consisting of alkylaminocarbonyl, alkoxyalkyl, and heteroaryl.

8. The compounds of claim 7 wherein X is selected from the group consisting of methoxymethyl and optionally substituted furanyl.

9. The compounds of claim 1 wherein Y is selected from the group consisting of aralkyl, aryl, alicyclic, and alkyl.

10. The compounds of claim 1 wherein each R^1 is independently selected from the group consisting of -H, alkyl, aryl, alicyclic where the cyclic moiety contains a carbonate or thiocarbonate, optionally substituted phenyl, optionally substituted benzyl, optionally substituted alkylaryl, $-C(R^2)_2OC(O)R^3$, $C(R^2)_2$-O-C(O)OR^3, $-C(R^2)_2$-OC(O)SR^3, -alkyl-S-C(O)R^3, alkyl-S-

S-alkylhydroxyl, and -alkyl-S-S-S-alkylhydroxy, or together R^1 and R^1 are alkyl-S-S-alkyl to form a cyclic group, or R^1 and R^1 together are



,

wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected to form a cyclic group containing 3-5 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected to form a cyclic group containing 3 carbon atoms substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, and aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH=CR^2R^2)OH$, $-CH(C\equiv CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl; and

R^9 is selected from the group consisting of alkyl, aralkyl, and alicyclic.

11. The compounds of claim 10 wherein each R^1 is independently selected from the group consisting of optionally substituted phenyl, optionally substituted benzyl, $-C(R^2)_2OC(O)R^3$, $-C(R^2)_2OC(O)OR^3$, and -H.

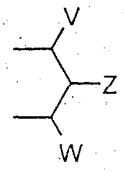
12. The compounds of claim 10 wherein R^1 is H.

13. The compounds of claim 10 wherein at least one R^1 is aryl, or $-C(R^2)_2$-aryl.

14. The compounds of claim 10 wherein at least one R^1 is $-C(R^2)_2-OC(O)R^3$, $-C(R^2)_2-OC(O)OR^3$, $-C(R^2)_2-OC(O)SR^3$.

15. The compounds of claim 10 wherein at least one R^1 is alkyl-S-S-alkylhydroxyl, -alkyl-S-$C(O)R^3$, and -alkyl-S-S-S-alkylhydroxy, or together R^1 and R^1 are alkyl-S-S-alkyl to form a cyclic group.

16. The compounds of claim 10 wherein together R^1 and R^1 are



to form a cyclic group;

wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected to form a cyclic group containing 3-5 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected to form a cyclic group containing 3 carbon atoms substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, and aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH{=}CR^2R^2)OH$, $-CH(C{\equiv}CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl; and

R^9 is selected from the group consisting of alkyl, aralkyl, and alicyclic.

17. The compounds of claim 16 wherein V and W both form a 6-membered carbocyclic ring substituted with 0-4 groups, selected from the group consisting of hydroxy, acyloxy, alkoxycarbonyloxy, and alkoxy; and Z is R^2.

18. The compounds of claim 16 wherein V and W are hydrogen; and Z is selected from the group consisting of hydroxyalkyl, acyloxyalkyl, alkyloxyalkyl, and alkoxycarboxyalkyl.

19. The compounds of claim 16 wherein V and W are independently selected from the group consisting of hydrogen, optionally substituted aryl, and optionally substituted heteroaryl, with the proviso that at least one of V and W is optionally substituted aryl or optionally substituted heteroaryl.

20. The compounds of claim 1 wherein together R^1 and R^1 are optionally substituted lactones attached at the omega position.

21. The compounds of claim 10 wherein R^1 is alicyclic where the cyclic moiety contains carbonate or thiocarbonate.

22. The compounds of claim 21 wherein together R^1 and R^1 are optionally substituted 2-oxo-1,3-dioxolenes attached through a methylene to the phosphorus oxygen.

23. The compounds of claim 1 wherein A is selected from the group consisting of $-NR^8_2$, and halogen;

E is selected from the group consisting of -H, halogen, -CN, lower alkyl, lower perhaloalkyl, lower alkoxy, and lower alkylthio;

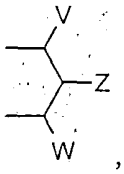
X is selected from the group consisting of alkylamino, alkyl, alkoxyalkyl, alkynyl, alkylthio, aryl, heteroaryl, alkylcarbonylamino, 1,1-dihaloalkyl, carbonylalkyl, alkyl(OH), alkyl(sulfonate), and alkylaminocarbonyl; and

R^4 and R^7 are selected from the group consisting of -H, and lower alkyl.

24. The compounds of claim 23 wherein

Y is selected from the group consisting of aralkyl, aryl, alicyclic, and alkyl.

25. The compound of claim 24 wherein R^1 and R^1 together are



V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected to form a cyclic group containing 3-5 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected to form a cyclic group containing 3 carbon atoms substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, and aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2{}_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH{=}CR^2R^2)OH$, $-CH(C{\equiv}CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl; and

R^9 is selected from the group consisting of alkyl, aralkyl, and alicyclic.

26. The compounds of claim 23 wherein A is $-NR^8{}_2$;

E is selected from the group consisting of -H, -Cl, and -SCH_3; and X is selected from the group consisting of optionally substituted furanyl and alkoxyalkyl.

27. The compounds of claim 26 wherein A is -NH_2; E is selected from the group consisting of -H, -Cl, and -SCH_3;

X is selected from the group consisting of 2,5-furanyl, and methoxymethyl; and

Y is lower alkyl.

28. The compound of claim 27 wherein E is -H, X is 2,5-furanyl, and Y is neopentyl.

29. The compound of claim 28 wherein R^1 is -CH_2O-C(O)-$C(CH_3)_3$ or its HCl salt.

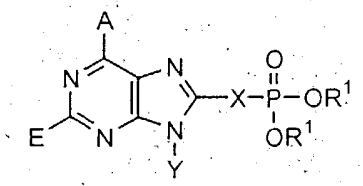
30. The compound of claim 27 wherein E is -SCH_3, X is 2,5-furanyl, and Y is isobutyl.

31. The compound of claim 30 wherein R^1 is -CH_2O-C(O)-$C(CH_3)_3$ or its HCl salt.

32. The compound of claim 27 wherein E is -H, X is 2,5-furanyl, and Y is 1-(3-chloro-2,2-dimethyl)-propyl.

33. The compound of claim 32 wherein R^1 is -CH_2O-C(O)-$C(CH_3)_3$ or its HCl salt.

34. A method of treating an animal for diabetes mellitus, comprising administering to said animal a therapeutically effective amount of a compound of formula (1):



wherein

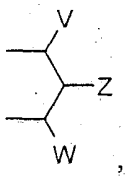
A is selected from the group consisting of -NR^8_2, $NHSO_2R^3$, -OR^5, -SR^5, halogen, lower alkyl, -$CON(R^4)_2$, guanidine, amidine, -H, and perhaloalkyl;

E is selected from the group consisting of -H, halogen, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and -NR^7_2;

X is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, *alkyl(carboxyl)*, *alkyl(hydroxy)*, *alkyl(phosphonate)*, *alkyl(sulfonate)*, *aryl*, *alkylaminoalkyl*, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or together with Y forms a cyclic group including cyclic alkyl, heterocyclic, and aryl;

Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2{}_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;

R^1 is independently selected from the group consisting of -H, alkyl, aryl, alicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl, alkylaryl, $-C(R^2)_2OC(O)NR^2{}_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, alkyl-S-$C(O)R^3$, alkyl-S-S-alkylhydroxy, and alkyl-S-S-S-alkylhydroxy, or together R^1 and R^1 are -alkyl-S-S-alkyl to form a cyclic group, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected to form a cyclic group containing 3-5 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected to form a cyclic group containing 3 carbon atoms substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, and aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH=CR^2R^2)OH$, $-CH(C\equiv CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together they form a bidendate alkyl;

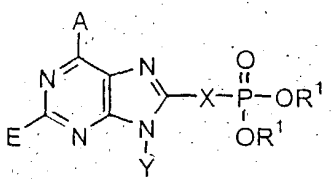
R^9 is selected from the group consisting of alkyl, aralkyl, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

35. A method of lowering blood glucose levels in an animal in need thereof, comprising administering to said animal a pharmaceutically acceptable amount of a compound of formula (1):



wherein

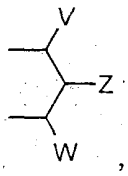
A is selected from the group consisting of $-NR^8_2$, $NHSO_2R^3$, $-OR^5$, $-SR^5$, halogen, lower alkyl, $-CON(R^4)_2$, guanidine, amidine, -H, and perhaloalkyl;

E is selected from the group consisting of -H, halogen, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or together with Y forms a cyclic group including cyclic alkyl, heterocyclic, and aryl;

Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;

R^1 is independently selected from the group consisting of -H, alkyl, aryl, alicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl, alkylaryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2$-OC (O)R^3, $C(R^2)_2$-O-C(O)OR^3, $-C(R^2)_2OC(O)SR^3$, alkyl-S-C(O)R^3, alkyl-S-S-alkylhydroxy, and alkyl-S-S-S-alkylhydroxy, or together R^1 and R^1 are -alkyl-S-S-alkyl to form a cyclic group, or together R^1 and R^1 are



,

wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected to form a cyclic group containing 3-5 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected to form a cyclic group containing 3 carbon atoms substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, and aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2{}_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH{=}CR^2R^2)OH$, $-CH(C{\equiv}CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together they form a bidendate alkyl;

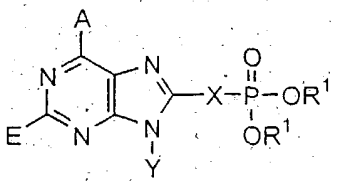
R^9 is selected from the group consisting of alkyl, aralkyl, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

36. A method of inhibiting FBPase at the AMP site in patients in need thereof, comprising administering to said patients an FBPase inhibitory amount of a compound of formula (1):



wherein

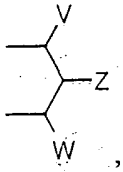
A is selected from the group consisting of $-NR^8_2$, $NHSO_2R^3$, $-OR^5$, $-SR^5$, halogen, lower alkyl, $-CON(R^4)_2$, guanidine, amidine, -H, and perhaloalkyl;

E is selected from the group consisting of -H, halogen, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or together with Y forms a cyclic group including cyclic alkyl, heterocyclic, and aryl;

Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;

R^1 is independently selected from the group consisting of -H, alkyl, aryl, alicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl, alkylaryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, alkyl-S-$C(O)R^3$, alkyl-S-S-alkylhydroxy, and alkyl-S-S-S-alkylhydroxy, or together R^1 and R^1 are -alkyl-S-S-alkyl to form a cyclic group, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and -R^9; or

together V and Z are connected to form a cyclic group containing 3-5 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected to form a cyclic group containing 3 carbon atoms substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, and aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of -CH_2OH, -CH_2OCOR^3, -$CH_2OC(O)SR^3$, -$CH_2OCO_2R^3$, -SR^3, -$S(O)R^3$, -CH_2N_3, -$CH_2NR^2_2$, -CH_2Ar, -CH(Ar)OH, -$CH(CH{=}CR^2R^2)OH$, -$CH(C{\equiv}CR^2)OH$, and -R^2;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is -R^2, then at least one of V and W is not -H or -R^9;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and -$C(O)R^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, -$C(O)R^{10}$, or together they form a bidendate alkyl;

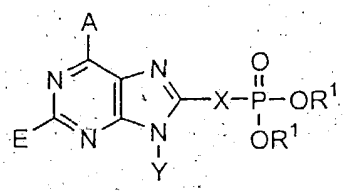
R^9 is selected from the group consisting of alkyl, aralkyl, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, -NH_2, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

37. A method of inhibiting gluconeogenesis in animal in need thereof, comprising administering to said animal an effective amount of a compound of formula (1):



wherein

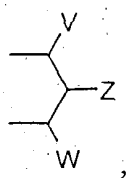
A is selected from the group consisting of $-NR^8_2$, $NHSO_2R^3$, $-OR^5$, $-SR^5$, halogen, lower alkyl, $-CON(R^4)_2$, guanidine, amidine, -H, and perhaloalkyl;

E is selected from the group consisting of -H, halogen, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or together with Y forms a cyclic group including cyclic alkyl, heterocyclic, and aryl;

Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;

R^1 is independently selected from the group consisting of -H, alkyl, aryl, alicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl, alkylaryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, alkyl-S-$C(O)R^3$, alkyl-S-S-alkylhydroxy, and alkyl-S-S-S-alkylhydroxy, or together R^1 and R^1 are -alkyl-S-S-alkyl to form a cyclic group, or together R^1 and R^1 are



wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected to form a cyclic group containing 3-5 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected to form a cyclic group containing 3 carbon atoms substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, and aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH{=}CR^2R^2)OH$, $-CH(C{\equiv}CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together they form a bidendate alkyl;

R^9 is selected from the group consisting of alkyl, aralkyl, and alicyclic;

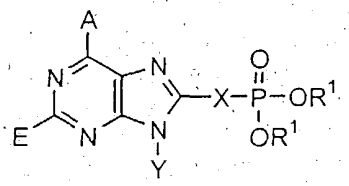
R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

38. A method of treating an animal for a disease derived from abnormally elevated insulin levels, comprising administering to said animal a therapeutically effective amount of a fructose-1,6-bisphosphatase inhibitor which binds to the AMP site of FBPase.

39. The method of claim 38 wherein said inhibitor is compound of formula (1):



wherein

A is selected from the group consisting of $-NR^8{}_2$, $NHSO_2R^3$, $-OR^5$, $-SR^5$, halogen, lower alkyl, $-CON(R^4)_2$, guanidine, amidine, -H, and perhaloalkyl;

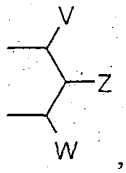
E is selected from the group consisting of -H, halogen, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7{}_2$;

X is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or together with Y forms a cyclic group including cyclic alkyl, heterocyclic, and aryl;

Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2{}_2$, and $-OR^3$,

all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;

R^1 is independently selected from the group consisting of -H, alkyl, aryl, alicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)2$-aryl, alkylaryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, alkyl-S-$C(O)R^3$, alkyl-S-S-alkylhydroxy, and alkyl-S-S-S-alkylhydroxy, or together R^1 and R^1 are -alkyl-S-S-alkyl to form a cyclic group, or together R^1 and R^1 are



,

wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected to form a cyclic group containing 3-5 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected to form a cyclic group containing 3 carbon atoms substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, and aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N^3$, $-CH_2NR^2_2$, $-CH_2Ar$, -CH(Ar)OH, $-CH(CH=CR^2R^2)OH$, $-CH(C\equiv CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together they form a bidendate alkyl;

R^9 is selected from the group consisting of alkyl, aralkyl, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

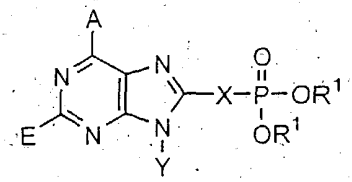
R^{11} is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

40. The method of claim 39 wherein said disease is atherosclerosis.

41. A method of treating an animal with excess glycogen storage disease, comprising administering to said animal in need thereof a therapeutically effective amount of a fructose-1,6-bisphosphatase inhibitor which binds to the AMP site of FBPase.

42. The method of claim 41 wherein said inhibitor is a compound of formula (1):



wherein

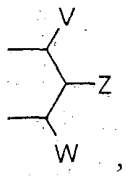
A is selected from the group consisting of $-NR^8_2$, $NHSO_2R^3$, $-OR^5$, $-SR^5$, halogen, lower alkyl, $-CON(R^4)_2$, guanidine, amidine, -H, and perhaloalkyl;

E is selected from the group consisting of -H, halogen, lower alkylthio, lower perhaloalkyl, lower alkyl, lower alkenyl, lower alkynyl, lower alkoxy, -CN, and $-NR^7_2$;

X is selected from the group consisting of alkylamino, alkyl, alkenyl, alkynyl, alkyl(carboxyl), alkyl(hydroxy), alkyl(phosphonate), alkyl(sulfonate), aryl, alkylaminoalkyl, alkoxyalkyl, alkylthioalkyl, alkylthio, alicyclic, 1,1-dihaloalkyl, carbonylalkyl, aminocarbonylamino, alkylaminocarbonyl, alkylcarbonylamino, aralkyl, and alkylaryl, all optionally substituted; or together with Y forms a cyclic group including cyclic alkyl, heterocyclic, and aryl;

Y is selected from the group consisting of -H, alkyl, alkenyl, alkynyl, aryl, alicyclic, aralkyl, aryloxyalkyl, alkoxyalkyl, $-C(O)R^3$, $-S(O)_2R^3$, $-C(O)-OR^3$, $-CONHR^3$, $-NR^2_2$, and $-OR^3$, all except H are optionally substituted; or together with X forms a cyclic group including aryl, cyclic alkyl, and heterocyclic;

R^1 is independently selected from the group consisting of -H, alkyl, aryl, alicyclic where the cyclic moiety contains a carbonate or thiocarbonate, $-C(R^2)_2$-aryl, alkylaryl, $-C(R^2)_2OC(O)NR^2_2$, $-NR^2-C(O)-R^3$, $-C(R^2)_2-OC(O)R^3$, $C(R^2)_2-O-C(O)OR^3$, $-C(R^2)_2OC(O)SR^3$, alkyl-S-C(O)R^3, alkyl-S-S-alkylhydroxy, and alkyl-S-S-S-alkylhydroxy, or together R^1 and R^1 are -alkyl-S-S-alkyl to form a cyclic group, or together R^1 and R^1 are



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wherein

V and W are independently selected from the group consisting of hydrogen, aryl, substituted aryl, heteroaryl, substituted heteroaryl, 1-alkenyl, 1-alkynyl, and $-R^9$; or

together V and Z are connected to form a cyclic group containing 3-5 atoms, optionally 1 heteroatom, substituted with hydroxy, acyloxy, alkoxycarboxy, or aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus; or

together V and W are connected to form a cyclic group containing 3 carbon atoms substituted with hydroxy, acyloxy, alkoxycarboxy, alkylthiocarboxy, hydroxymethyl, and aryloxycarboxy attached to a carbon atom that is three atoms from an oxygen attached to the phosphorus;

Z is selected from the group consisting of $-CH_2OH$, $-CH_2OCOR^3$, $-CH_2OC(O)SR^3$, $-CH_2OCO_2R^3$, $-SR^3$, $-S(O)R^3$, $-CH_2N_3$, $-CH_2NR^2_2$, $-CH_2Ar$, $-CH(Ar)OH$, $-CH(CH=CR^2R^2)OH$, $-CH(C\equiv CR^2)OH$, and $-R^2$;

with the provisos that:

a) V, Z, W are not all -H; and

b) when Z is $-R^2$, then at least one of V and W is not -H or $-R^9$;

R^2 is selected from the group consisting of R^3 and -H;

R^3 is selected from the group consisting of alkyl, aryl, alicyclic, and aralkyl;

R^4 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, and lower aryl;

R^5 is selected from the group consisting of lower alkyl, lower aryl, lower aralkyl, and lower alicyclic;

R^6 is independently selected from the group consisting of -H, and lower alkyl;

R^7 is independently selected from the group consisting of -H, lower alkyl, lower alicyclic, lower aralkyl, lower aryl, and $-C(O)R^{10}$;

R^8 is independently selected from the group consisting of -H, lower alkyl, lower aralkyl, lower aryl, lower alicyclic, $-C(O)R^{10}$, or together they form a bidendate alkyl;

R^9 is selected from the group consisting of alkyl, aralkyl, and alicyclic;

R^{10} is selected from the group consisting of -H, lower alkyl, $-NH_2$, lower aryl, and lower perhaloalkyl;

R^{11} is selected from the group consisting of alkyl, aryl, -OH, $-NH_2$ and $-OR^3$; and

pharmaceutically acceptable prodrugs and salts thereof.

43. The method of claims 34, 35, 36, 37, 38, 39, 40, 41, or 42 wherein said compound is administered orally.